

**REMARKS**

Claim 3 is presently pending in the application.

Claims 1-2 and 4-10, withdrawn from consideration by the Examiner as being directed to a non-elected invention, have been canceled without prejudice to the filing of a divisional application directed to the subject matter thereof.

Claim 3 has been amended to more clearly recite the elements of the inventive device and the relationships between them. Claim 3 now clearly recites that a determination of hydrogen peroxide in body fluid is made based on a measurement of chemiluminescence intensity. The photomultiplier originally in claim 3 has been moved to new dependent claim 11, because it is not essential to measure hydrogen peroxide, but is useful, for example, when the light is very weak. Support for this amendment may be found, for example, at page 2, lines 11-21, page 3, line 15 to page 4, line 5, and in Fig. 1 of the specification. No new matter has been added by this amendment, and entry is respectfully requested.

Applicants acknowledge and appreciate the Examiner's indication in the present Office Action that the presently claimed invention is patentable over the prior art of record. However, the Examiner has rejected claim 3 under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement and has rejected claim 3 under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse these rejections and the arguments in support thereof as follows, and respectfully request reconsideration and withdrawal of the rejections.

**The Present Invention**

The presently claimed invention is directed to a novel and quantitative chemiluminescence system using a flow cell packed with immobilized horseradish peroxidase (HRP) for determining the concentration of hydrogen peroxide in body fluid. The presently claimed device contains two mobile phase passages, two chromatography pumps, an autosampler, a joined flow passage, and a chemiluminometer having a flow cell in which a HRP immobilized stationary phase is packed. As described in the specification at page 4, lines 9-12,

the mobile phase and flow passages are simply tubes, such as Teflon® or stainless steel, which can transport liquids.

In the presently claimed device, an autosampler collects a sample of body fluid, which is then pumped by a first chromatography pump into a first mobile phase passage or tube. A second chromatography pump is used to inject a solution of imidazoles and an alkaline buffer into a second mobile phase passage or tube. These two tubes are then joined together into a single tube, designated as a flow passage, which transports the body fluid and the imidazoles and alkaline buffer solution into the flow cell of a chemiluminometer. In the flow cell, which is packed with a HRP immobilized stationary phase, the body fluid, the imidazoles, and the alkaline buffer are mixed together and react with the immobilized HRP.

In a preferred embodiment, the reaction mechanism of the chemiluminescence, which occurs in the flow cell of the chemiluminometer, first involves the immobilized HRP, the hydrogen peroxide, and dissolved oxygen, which, in the presence of the alkaline buffer, oxidizes the imidazole to imidazole hydroperoxide. The imidazole hydroperoxide is then further oxidized to imidazole dioxetane, which emits light while decaying (see, for example, page 6, lines 1-6 of the specification). The intensity of the light emitted by this reaction is measured by a photomultiplier of the chemiluminescence detecting system.

As will be appreciated by one skilled in the art, the presently claimed invention is essentially directed to the use of liquid chromatography to detect a compound, hydrogen peroxide, based on the chemiluminescence reaction which takes place in the flow cell. The novel component of the presently claimed device is a flow cell in which a HRP immobilized stationary phase is packed, thereby utilizing HRP as the light emitter. This light emitter, which is not a chemiluminescent molecule, is different from the commonly used chemiluminescent luminal, isoluminol, lophine, lucigenin and peroxyxalate, which have conventionally been used as light emitters to determine hydrogen peroxide by chemiluminescence (see, for example, page 1, lines 10-14 of the specification).

*Rejection under § 112, first paragraph*

In support of the rejection of claim 3 under 35 U.S.C. § 112, first paragraph, the Examiner contends that the specification fails to describe the apparatus structure in sufficient detail and that the drawings fail to show the apparatus structure. Applicants respectfully but strenuously traverse this rejection for the reasons set forth in detail below.

As shown in Fig. 1 and described at page 3, lines 24-27, the presently claimed invention uses two high performance liquid chromatography pumps 11, 21, an autosampler 12, and a chemiluminometer 31 with a flow cell 32. These components are all commonly used in chemiluminescence devices and preferred components are described at page 5, lines 16-23 of the specification. Enclosed herewith are drawings from the technical manuals of a representative chemiluminometer, autosampler, and HPLC pump, manufactured by JASCO Corporation. However, the presently claimed device is not limited to such devices. Rather, since all of the aforementioned components are commonly used devices in an apparatus for a chromatographic and chemiluminescence analysis, their structure, operation, and functionality are commonly known to one skilled in the art and, as such, the apparatus structure of the presently claimed device is readily understandable by one skilled in the art. Accordingly, reconsideration and withdrawal of the § 112, first paragraph rejection are respectfully requested.

*Rejection under § 112, second paragraph*

The Examiner takes the position that claim 3 is indefinite because the following elements are allegedly uncertain or unclear: the meaning and scope of the expression “mobile phase passage for body fluid”; the purpose of chromatography and its functionality in the presently claimed invention for determining hydrogen peroxide; the differences between the first and second mobile phase passages and their functionality together with respect to a pump and chromatography; and the functionality of the chemiluminometer with respect to the first and second mobile phase passages, pumps, and chromatography to determine hydrogen peroxide. Applicants respectfully but strenuously traverse this rejection for the reasons set forth in detail below.

As explained in the specification at page 4, lines 9-12, the “mobile phase passages” are simply tubes for transporting liquids. Exemplary materials for such tubes are Teflon® and

stainless steel. It is also noted that the expression “mobile phase passage” is commonly used with respect to chemiluminescence and chromatography analyses and, as such, will be readily understood by one skilled in the relevant art.

Claim 3 clearly recites that a first chromatography pump injects body fluid into a first mobile phase passage and a second chromatography pump is used to inject a solution of imidazoles and an alkaline buffer into a second mobile phase passage. The two mobile phase passages are different in that one is used to transport the bodily fluid and the second is used to transport the imidazole/alkaline buffer solution; the two chromatography pumps are used to inject the respective liquids into the mobile phase passages. These two tubes are then joined together into a single tube, designated as a flow passage, which transports the body fluid and the imidazoles and alkaline buffer solution into a flow cell of a chemiluminometer, where the intensity of light emitted by the immobilized HRP is measured. This measurement corresponds to the concentration of hydrogen peroxide in the body fluid (see, for example, page 6, lines 7-13 of the specification).

Chromatography involves passing a mixture or solution which contains an analyte through a stationary phase, which separates it from other molecules in the mixture and allows it to be isolated. Thus, chromatography pumps are used because this is essentially the chromatographic analysis of a chemiluminescence reaction. As well understood by one skilled in the art, chemiluminescence detection is commonly used in a chromatography analysis when there is a need to detect compounds with a high degree of sensitivity (see, for example, page 1, lines 10-11 of the specification). In the presently claimed device, chromatographic analysis is performed using a novel flow cell packed with a HRP immobilized stationary phase to measure the concentration of hydrogen peroxide in body fluid with high sensitivity.

Since all of the aforementioned components are commonly used devices in an apparatus for a chromatographic and chemiluminescence analysis, their individual and combined functionalities would be readily understandable by one skilled in the art. Accordingly, reconsideration and withdrawal of the § 112, second paragraph rejection are respectfully requested.

Based on the preceding amendments and remarks, it is respectfully submitted that the pending claim is in full compliance with § 112 and in condition for allowance. A Notice of Allowance is respectfully requested.

Respectfully submitted,

**Emiko Kaneko et al.**

September 27, 2006 By: Hanff Schway, Reg. No. 25,918  
(Date) *for* SANDRA M. KATZ

Registration No. 51,864

AKIN GUMP STRAUSS HAUER & FELD LLP

One Commerce Square  
2005 Market Street, Suite 2200  
Philadelphia, PA 19103-7013  
Telephone: 215-965-1200

**Direct Dial: 215-965-1344**

Facsimile: 215-965-1210

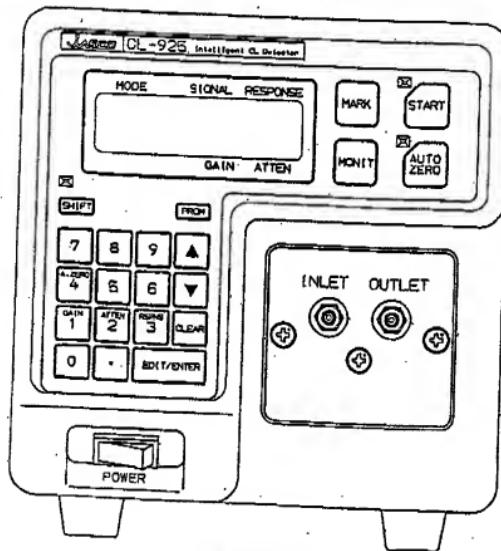
E-Mail: skatz@akingump.com

SMK:BS:cmb  
7633834

Encl: Diagrams from Technical Manuals of JASCO Chemiluminometer, Autosampler, and  
HPLC Pump

## JUSCO GULLIVER SERIES

### CL-925型 インテリジェント化学発光検出器 (Ver.1.xx) 取扱説明書



日本分光

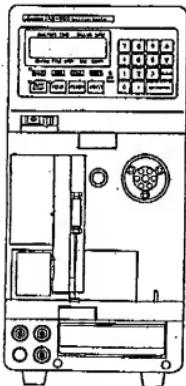
P/N:0301-1257A

作成 1995.11

Chemiluminescence made by JASCO Corporation

## JASCO GULLIVER SERIES

AS-950 型  
インテリジェントオートサンプラー  
取扱説明書  
操作編  
(ROM VERSION 1.xx)



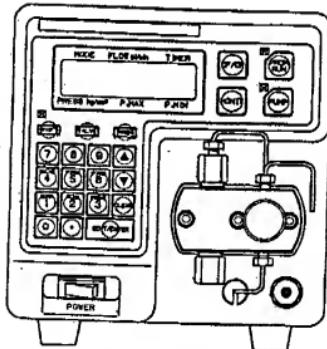
日本分光

作成 1992.11

Autosampler made by JASCO corporation

## JASCO GULLIVER SERIES

PU-980 型  
インテリジェント HPLC ポンプ  
取扱説明書  
保守編  
(機番 Bxxxxxxxx~)



日本分譲

作成 1992.10

HPLC pump made by JASCO Corporation